Clinical epidemiological study of employees exposed to surfactant blend containing perfluorononanoic acid

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ORIGINAL ARTICLE

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Introduction: An epidemiological study was conducted of a perfluorononanoic acid (PFNA) surfactant blend, to investigate whether clinical differences were apparent between employees who were potentially exposed to the surfactant and those who were not exposed. The surfactant blend, which is related to other previously studied perfluorinated materials, is used in the production of some high-performance polymers.

Methods: All 630 individuals employed at a polymer production facility using PFNA (CAS No 72968-38-8) at any time between 1 January 1989 and 1 July 2003 were included in the cohort. Plausibly related laboratory test results were abstracted from annual medical examination records, including liver enzyme function and blood lipids. Detailed work histories, available for all employees, provided the basis for determining exposure category. Thirty two clinical parameters were evaluated by exposure level at five points in time, determined to reflect changes in possible exposure intensity, as well as greatest number of records available. Annual cross-sectional analyses and longitudinal analyses that accounted for multiple measurements per person were conducted separately for men and women, by exposure groups.

Results: Differences by exposure group for all laboratory measures, adjusted for age and body mass index, were small and not clinically significant. Although some statistically significant pair-wise differences were observed, these observations were not consistent between men and women, or over the five analysis windows. For the seven outcome variables (liver enzymes and blood lipids) examined in separate longitudinal models, no significant increase or decrease was observed by unit increase in cumulative exposure intensity score.

Conclusion: This is the first epidemiological study investigating the possible health effects in humans associated with exposure to PFNA blend. Based on laboratory measures assessed over more than a decade, no adverse clinical effects were detected from occupational exposure to PFNA blend.

For more than a decade, the public health relevance of exposure to perfluorooctanoic acid (PFOA or C8) has been examined because of its biological persistence and the lack of information on possible long-term health implications. PFOA has been detected in blood bank samples across the US as well as in individuals across the globe (World Wildlife Fund, 2004).[1] A related long-chain fluorinated hydrocarbon, perfluorononanoic acid (PFNA or C9), is the principal carbon chain-length in a surfactant or ''slip-agent'' blend (CAS No 72968-38-8) used in the production of some high-performance polymers. The remaining fluorinated hydrocarbons in the blend consist primarily of C11 and C13 congeners. Because the perfluorinated compounds in the blend may also persist biologically, management of a chemical production facility using this blend was interested in whether measurable health effects were associated with employee exposures. A limited number of toxicological studies have been conducted by the manufacturers and users of PFNA, and no epidemiological studies have been published to date. Therefore, the limited toxicological data on PFNA and the epidemiological findings regarding the related compound, PFOA, served to frame the research questions.

A 90-day rat PFNA feeding study with a 60-day recovery period suggested that the liver was the main target organ, with effects on serum clinical chemistry, higher liver weights, and evidence of peroxisome proliferation in both males and females. Microscopic lesions in the liver and gastrointestinal tract were noted in the male rats. At the end of the recovery period most of the affected parameters had partially or completely returned to normal. The enhanced effect in the males was consistent with the observed higher serum levels of the surfactant (WIL Research Laboratories, LLC. Study number WIL-497002, 2006). Similarly, toxicity studies of PFOA in animals have shown effects on lipid metabolism (for example, reduction of serum cholesterol) and changes in liver function (for example, hepatic enzyme tests).[2]

The epidemiological investigations conducted at plant sites where PFOA is either manufactured or used in polymer production provided additional guidance for relevant clinical hypotheses. Two studies that evaluated possible liver effects associated with PFOA exposure in a polymer production area found no impairment of liver function based on blood liver function tests (DuPont, 1981, 1983). Similarly, studies of 3M employees found no excess of liver cancer deaths attributable to PFOA (University of Minnesota School of Public Health, 2001),[3 4] and no changes in liver function parameters were observed.[5] A more extensive study of serum concentration of perfluorooctanesulfonate (PFOS), another C8 fluorocarbon compound, found no association with changes in blood clinical chemistries or haematology after adjusting for other clinical measures, such as age and lifestyle factors.[6] This study was consistent with studies of PFOA exposures, finding no adverse changes in blood chemistries (that is, markers of disease) or increases in cancer mortality.

Based on the positive findings for liver and blood lipid changes in rats exposed to PFNA blend, and the choice of blood chemistry tests evaluated in the epidemiological studies of a similar compound, PFOA, the current study evaluated a number of clinical laboratory measurements collected over a period of more than 25 years among employees of a US

Abbreviations: PFOA, perfluorooctanoic acid; PFNA, perfluorononanoic acid

production facility using the PFNA blend. The facility, which manufactures a variety of chemicals and polymers, is located in a rural area, and employees typically reside in communities near the plant. The study was designed to identify whether any differences in clinical measures could be identified between employees in surfactant-exposed jobs compared to employees in non-exposed jobs.

METHODS

All individuals ever employed at the facility at any time between 1 January 1989 and 1 July 2003 were eligible to be included in the study cohort. This start date was selected because medical data were known to be complete beginning in 1989, and computerisation of existing employment records began in the early 1990s. The study protocol was reviewed by a federally (US) registered institutional review board.

Complete work history, date of birth, gender and race were available for all individuals actively employed at the facility for at least one day between 1 January 1989 and 1 July 2003. Employment data were available since the plant opened in 1949, allowing complete reconstruction of employment histories for all cohort members hired before the study start date.

Starting in 1989, annual medical examinations were conducted, generally around the anniversary of an employee's date of hire, and nearly all medical records were located. Exams were also provided at entry, retirement and to those re-hired after lay-off. Many employees had medical records generated before 1989—some going back to 1957—but these early records were not uniformly available or complete. There is no documented rationale or systematic pattern identified to explain missing records prior to 1989.

Records were abstracted for height, weight, date of exam, and 32 clinical chemistry variables (calcium, phosphorus, sodium, potassium, chloride, alkaline phosphatase, total protein, albumin, globulin, creatinine, glucose, iron; A/G ratio, BUN, BUN/creatinine LDH, AST, ALT, GGT, total bilirubin, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol, total cholesterol/HDL ratio, LDL/HDL ratio, TSH, thyroxine (T4), T3 uptake, free thyroxine index, uric acid). Three laboratories had been used by the company since 1989, and a fourth lab was used from 1976–88. We used the reference ranges from the laboratory used for the greatest number of years, which was also the most recent laboratory used by the plant, to identify values that could be considered abnormal.

Complete work histories were available for all employees. Each job record provided: date of hire into the company, job title, start date for specific job, job and location codes. Working with plant staff, all job titles were reviewed to identify those with potential surfactant exposure, and to consolidate multiple job titles that occurred for the same job over time. Employees with jobs in maintenance or technical positions were considered exposed to surfactant, though at a lower level than the process workers and other workers in the building manufacturing the polymer. A non-exposed group consisted of administrative jobs and jobs in various other production processes at the facility that did not use the PFNA blend and worked in different buildings at the plant site. The final classification consisted of three exposure categories: high exposure (process job titles); low exposure (finishing, supervisory, lab, clerk, maintenance, and technical job titles); and no exposure (other processes, administrative job titles).

A variable representing the highest exposure level achieved by a worker was created using the final three surfactant exposure categories. Assignment to the exposure categories was hierarchical and mutually exclusive at any particular point in time. That is, once an employee was in a ''high'' exposure process job, his or her exposure was considered ''high'' for that year, and subsequent years. It is possible for an employee assigned to ''low'' or ''no exposure'' to move to a higher exposure group over time in the analysis, but not the reverse.

Before the start of the epidemiological study, the company had obtained blood samples from a subset of current employees who worked in various areas of the plant, to ascertain whether PFNA levels could be detected in the blood. These limited biomonitoring results were used to validate the exposure categories generated based on the occupational history, but were insufficient to be used in any analyses.

Three main analyses were conducted. First, a cross-sectional analysis was conducted to evaluate differences in average values of all 32 clinical laboratory measures at five points in time. Additional annual cross-sectional analyses of mean lab values by exposure groups and longitudinal analysis accounting for multiple measurements per person were also conducted. Analyses used the three exposure groups for men and two groups for women, combining ''high'' and ''low'' because few women worked in the process area historically. All analyses were adjusted for age and body mass index (BMI), used as continuous variables. All analyses were conducted in SAS 8.0 (SAS Institute, Cary, NC, USA).

Five time periods were selected for cross-sectional analysis based on the following: (a) the earliest year (1976) sufficient clinical chemistry data were available for analysis; (b) the year (1989) complete medical records became available from the facility; (c) the year (1995) a liquid solution started to replace the powder form of surfactant; (d) the year (1998) following complete conversion of surfactant from powder to solution; (e) the latest year (2001) with sufficient data for analysis. Each time period, or analysis ''window'' encompassed a two-year period around the five key dates in order to capture the annual physical examination for each employee, and to reflect different exposure potential. For example, the 1989 period is believed to be indicative of the entire period when powdered surfactant blend (with potential for airborne dust exposure) was used, whereas the 1995 period would reflect lower potential airborne dust exposures. Many employees contribute data in multiple analysis windows. Laboratory test results dated closest to the mid-point of each analysis window were evaluated by exposure groups. Pairwise comparisons of adjusted means of each lab test were made across exposure groups in each analysis window using PROC GLM in SAS.

Based on findings in rats that liver enzymes and blood lipids may be the most likely to show any effects from exposure, adjusted annual means for these tests results by exposure group were graphed separately for men and women, using all years with data available. As with the analysis windows, each consecutive year does not represent the exact same group of individuals, because of the dynamic workforce, with substantial overlap from year to year.

Data used in the longitudinal analysis included annual measures of liver enzymes and blood lipids, age at entry into the cohort, annual measures of BMI, a weighted cumulative intensity score (up to the month before the annual exam) and the exposure group (none or any) in the month before the annual exam. A variable reflecting cumulative exposure to surfactant was also created. Each subject was assigned an annual weighted cumulative intensity score, where exposure intensity was quantified as 0 while not exposed, 1 during low exposure, and 2 during high exposure. Weighting was based on the proportion of each year spent in each exposure category. In addition, an indicator variable was created for powder or liquid surfactant use at the time of the annual exam. The general approach to the modelling was a mixed or random effects model. All longitudinal analyses used PROC MIXED in SAS.

Table 1 Descriptive characteristics of cohort at each of five cross-sections in time

		1976, n (%*)	1989, n (%*)	1995, n (%*)	1998, n (%*)	2001, n (%*)
Gender						
Men		163 (96)	289 (89)	323 (86)	289 (86)	261 (85)
Women		6 (4)	35 (11)	52 (14)	47 (14)	45 (15)
Race/ethnicity						
White		144 (97)	284 (94)	346 (92)	308 (92)	277 (91)
Black		3 (2)	17 (6)	26 (7)	25 (7)	28 (9)
Other		1 (1)	2 (<1)	3 (1)	3 (1)	1 (<1)
Exposure category						
Surfactant-high		14 (8)	35 (11)	34 (9)	35 (10)	30 (10)
Surfactant-low		104 (62)	206 (64)	259 (69)	234 (70)	224 (73)
No surfactant		51 (30)	83 (26)	82 (22)	67 (20)	52 (17)
Exposure category		Mean	Mean	Mean	Mean	Mean
Men						
Age	High	40.4	51.0	53.9	53.2	51.6
	Low	38.3	47.2	47.4	47.8	47.0
	None	40.2	47.8	47.8	48.4	47.6
BMI	High	25.0	26.3	27.3	27.8	28.8
	Low	25.6	26.9	28.1	28.1	29.2
	None	25.7	27.2	29.4	29.7	30.4
Years employed	High	14.6	24.8	27.8	27.4	25.0
	Low	11.7	19.9	18.8	18.8	17.0
	None	12.7	20.2	19.2	18.3	17.7
Women						
Age	Exposed	–	34.6	37.8	42.2	42.6
	None	–	41.8	45.4	47.0	48.1
BMI	Exposed	–	27.0	26.9	27.9	27.9
	None	–	24.9	26.8	28.2	28.4
Years employed	Exposed	–	8.1	9.1	13.0	12.3
	None	–	11.7	11.4	12.9	13.4

*May not add to 100% due to rounding.

RESULTS

As of 1 July 2003, a total of 269 men and women were actively employed at the facility. An additional 361 former employees, primarily retirees, were identified as having left the facility between 1 January 1989 and 30 June 2003. Medical and laboratory reports could not be located for 15 (2%) of the 630 eligible employees. Nineteen individuals with only one annual physical examination and employed less than one month were excluded, as well as one person who retired before 1989. For three individuals, gender could not be determined from the records or first name, leaving 518 men and 74 women with sufficient data for analysis. Descriptive results stratified by the five cross-sectional analysis windows are presented in table 1.

Means for all 32 laboratory measures were compared pairwise among high, low and no exposure groups for each of the five analysis windows; a linear trend test of means was also calculated for each lab measure for men. Adjusted group means for liver enzymes and blood lipids among men, as available, are presented in table 2; results for women are in table 3. The few statistically significant differences are noted in the table. Overall, differences among exposure groups for all lab tests were small, and not clinically significant. Although some statistically significant pairwise comparisons were observed, these observations were not consistent between men and women, or over the five analysis windows.

In the extended cross-sectional analysis for men and women, adjusted mean values of liver enzyme and blood lipid tests for each exposure group were plotted by year, from 1976 through 2003. Only years having at least five individuals with a particular laboratory test result were plotted. Values tended to fluctuate slightly across exposure groups over the years; no group mean was consistently elevated or depressed over the years available. For some lab measures, dips and peaks over time were observed; however, these shifts appeared to coincide with changes in laboratories used to test the blood.

Table 4 provides a selection of results from the longitudinal analysis for cholesterol and triglycerides. Too few data were available for stable models using data from the women only. The best fitting models included a variable for age, time, and BMI, as well as cumulative exposure intensity score, exposure status for a given year, and form of surfactant in use at the time of medical exam. BMI was strongly correlated with blood lipid levels in particular, and in the longitudinal analysis both BMI and age were independent predictors of each of the outcomes evaluated. For the seven outcome variables examined in separate models (total cholesterol, GGT, AST, ALT, alkaline phosphatase, bilirubin, triglycerides), no significant increase or decrease was observed by unit increase in exposure intensity score. The statistical interaction of ''current exposure'' and surfactant form (powder vs liquid) was statistically significant for some lab values; however, the direction of the association in these instances was opposite that hypothesised.

DISCUSSION

This is the first epidemiological study to investigate the possible association between exposure to PFNA surfactant blend and routine clinical laboratory results. As with previous studies of individuals occupationally exposed to a related compound, PFOA,[5–7] no clear impacts on clinical chemistry values were found. In the current study, all individuals who had worked in the facility at some time between 1989 and 2003 were included in the study, eliminating any possible selection bias associated with voluntary participation. Additionally, the stability of the cohort (based on low employee turnover and longevity of employment), and the large database of annual examinations provided by the company, allowed for nearly complete annual clinical and laboratory data. Some cohort members had more than 20 annual medical exams while employed at the facility. This considerable database provided sufficient data to allow us to conduct reasonably powerful longitudinal analyses capable of detecting small true differences.

Our analyses included a larger number of employees with multiple years of laboratory measures (78% of 518 men in the study cohort) than any previously published study of

Table 2 Comparison of adjusted mean lab values (liver enzymes, blood lipids) across exposure groups in men, 1976, 1989, 1995, 1998 and 2001

		Cross-sectional year*				
Laboratory measure	**Exposure level**	**1976**	**1989**	**1995**	**1998**	**2001**
LDH	High	177.7	145.7	156.1	149.2	165.0
	Low	179.7	148.4	159.2	151.1	164.9
	None	187.3	148.4	157.9	151.7	160.9
AST	High	32.2	27.0	23.4	23.5	33.5
	Low	30.5	29.1	23.9	22.5	27.2
	None	31.5	27.6	22.8	21.5	24.3
ALT	High	45.9†	29.8	21.4	26.0	37.6†††
	Low	38.0	34.1	24.4	25.8	33.1
	None	40.0	33.6	22.8	24.9	28.2
Bilirubin	High	0.58	0.52	0.59	0.67	0.62
	Low	0.57	0.51	0.69	0.74	0.61
	None	0.59	0.52	0.68	0.66	0.57
GGT	High	20.0	23.5	38.5	42.3	41.6
	Low	15.3	25.5	34.8	37.6	39.2
	None	20.9	30.0	37.6	33.8	35.7
Alkaline phosphatase	High	26.1	101.5	94.0	82.0†††	99.4
	Low	28.1	100.1	88.6	76.9	95.2
	None	29.1	97.0	86.6	72.1	91.2
Cholesterol (total)	High	239.8**†	241.4**†	215.6	221.9	211.9
	Low	207.7††	211.7††	203.3	205.4	202.9
	None	227.8	227.1	206.7	209.5	199.7
Triglycerides	High	231.9	204.2	204.7	202.3	175.1
	Low	195.6	168.9	167.7	183.1	182.0
	None	197.2	174.3	164.2	177.9	172.3
HDL	High	NA	51.5	37.2	44.6	44.3
	Low	NA	50.1	38.1	42.6	41.9
	None	NA	49.8	37.5	43.0	42.6
LDL	High	NA	147.0	142.9	142.2	134.7
	Low	NA	130.8	134.0	130.8	127.0
	None	NA	137.7	138.5	135.8	122.3
VLDL	High	NA	NA	30.4	34.1	29.1
	Low	NA	NA	26.7	30.6	30.9
	None	NA	NA	28.9	30.7	34.1

NA, not complete for early years.
*Number per exposure group (H, high; L, low; N, none): 1976 (14 H, 104 L, 45 N); 1989 (33 H, 198 L, 58 N); 1995 (30 H, 239 L, 54 N); 1998 (29 H, 220 L, 40 N); 2001 (23 H, 208 L, 30 N).
**Significance of group mean differences adjusted for age and body mass index is $p<0.05$.
†Pairwise differences between high and low; ††pairwise differences between low and none; †††pairwise differences between high and none.

Table 3 Comparison of adjusted mean lab values (liver enzymes, blood lipids) for women in exposed and unexposed groups, 1989, 1995, 1998 and 2001

		Cross-sectional year*			
Laboratory measure	**Exposed**	**1989**	**1995**	**1998**	**2001**
LDH	Yes	148.7	151.5	144.8	160.0
	No	148.1	162.4	149.4	182.8
AST	Yes	28.1	18.8	17.9	22.2
	No	24.8	20.1	18.2	21.0
ALT	Yes	30.1	14.4	15.9	20.4
	No	27.0	15.3	15.9	20.3
Bilirubin	Yes	0.37	0.51	0.57	0.43
	No	0.37	0.55	0.56	0.47
GGT	Yes	21.9	21.4	21.9	21.8
	No	12.6	54.6	32.8	35.0
Alkaline phosphatase	Yes	89.8	70.6	66.2	82.1
	No	76.7	74.9	68.9	92.4
Cholesterol (total)	Yes	182.5	177.3	197.4	203.4
	No	194.7	217.3	225.7	220.7
Triglycerides	Yes	81.1	103.2	112.3	111.5
	No	87.5	158.6	149.0	165.9
HDL	Yes	61.4	46.8	52.8	59.0
	No	63.8	52.4	59.7	56.3
LDL	Yes	91.3	109.5	122.1	121.6
	No	118.7	130.8	133.0	131.5
VLDL	Yes	NA	20.5	22.4	22.0
	No	NA	20.2	21.9	29.2

NA, not complete for early years.
*Number per exposure group (Y, exposed; N, not exposed): 1989 (10 Y, 25 N); 1995 (24 Y, 28 N); 1998 (20 Y, 27 N); 2001 (23 Y, 22 N).
Group mean differences adjusted for age and body mass index. No comparisons were significant at the $p<0.05$ level.

Table 4 Estimated effects of surfactant exposure on total cholesterol and triglycerides*

Effect	Change in total cholesterol	Standard error (95% CI)
1 unit change in cumulative exposure intensity score	−0.257	0.135 (−0.521 to 0.006)
Current exposure, by operating condition:		
Powder	−2.0109	1.5587 (−5.066 to 1.044)
Non-powder	1.4807	1.6898 (−1.831 to 4.793)
Effect	Change in triglycerides	Standard error (95% CI)
1 unit change in cumulative exposure intensity score	−1.054	0.5813 (−2.193 to 0.085)
Current exposure, by operating condition:		
Powder	4.1465	6.935 (−9.446 to 17.739)
Non-powder	16.0581	7.4959 (1.366 to 30.750)

*Estimates adjusted for time, age, and body mass index.

occupational exposure to perfluorinated compounds. The longitudinal modelling was a powerful analysis that included parameters to account for: (1) randomness in the outcome due to the subject measured; and (2) correlation between measurements made on the same subject. This analysis was sufficiently robust to detect small changes in lab means between exposure groups, as indicated by the precision in the interval estimates.

Studies of rats exposed to PFOA, a related fluorinated hydrocarbon compound, have indicated the liver may be a key target organ for toxicity, as well as lipid metabolism as a response indicator.[2] Weight loss (wasting) has also been reported in rats. Similar toxicity and wasting results in rats exposed to PFNA have also been reported (WIL Research Laboratories, 2006). The toxicokinetics of PFNA are currently unknown. Because no studies of PFNA exposure in humans have been published, studies of PFOA and PFNA effects in animals provided the basis for hypothesising effects on liver enzymes and blood lipids. If the rat data were indicative of possible human toxicity, the expected findings for the current study would include elevated liver enzymes among the exposed employees, as well as decreased cholesterol and triglycerides. Such results were not found in this study for either men or women.

In humans, several factors other than occupational chemical exposure are likely to impact liver enzymes or blood lipids, including age, medications, dietary supplements, existing disease, weight, family history and alcohol abuse. Potential confounding factors are unknown, as such factors would, by definition, be risk factors for liver enzyme or blood lipid changes that are also correlated with PFNA exposure. Our analyses controlled for age and BMI; data were inconsistently available for other exposures. Although information on alcohol use was not available, we examined the ratio of AST/ALT (aspartate transaminase, alanine transaminase) for values greater than 1.5, as an indicator of possible alcohol-related liver disease. Results of this analysis were negative. Anecdotally, alcohol use in this population is believed to be very low and infrequent—due to prevailing religious beliefs in the plant community. Alcohol is not sold in the community in which the facility is located or in several surrounding communities, which also is likely to contribute to lower use. Further, regular random drug and alcohol testing conducted at the facility may deter alcohol abuse. Tobacco use was not obtained for all individuals, however, it is unlikely that use would affect liver enzymes or blood lipids.

Although different laboratories were used by the company over the course of the study period, we do not consider this to be a serious limitation. For the cross-sectional analyses we were interested in the differences among the groups at a given point in time, and any variation introduced by various labs used over time would not matter. For any given year, all employee blood drawn for testing was sent to the same lab. The longitudinal analysis used values from different labs over time, and for the earliest years of analysis some additional variability may have been introduced. However, given that all blood values for a given year were reported from a single lab, the relative position of individuals, including by exposure category, would have been preserved.

Extreme values for any of the 32 clinical tests were examined at the individual level by a senior occupational physician, who was blind to exposure status. Initially, extreme values were defined as those outside the reference range of values as specified in the most recent laboratory reports (LabCorp 2002). For any extreme test results, the full medical record for these individuals was reviewed. In each instance, valid medical explanations for the extreme values were obtained from the record. In no instance could extreme values be attributed to high levels of exposure.

Based on rat studies, changes would be expected to occur in blood chemistries from long-term PFNA exposure. However, it is unknown in humans whether any potential changes in blood chemistries due to PFNA exposure would occur immediately upon exposure, after some lag period, or would require the exceeding of some threshold of cumulative exposure. We hypothesised that an effect, if one existed, would be during the time period when the surfactant was used in powder form. Before converting to a liquid suspension, those working in the process area would have had the highest potential for exposure, as the surfactant was manually measured and added to the process. With transition to the liquid form, exposure to the surfactant was more controlled. However, annual cross-sectional analyses of all 32 laboratory measures by exposure group showed no impact on blood chemistries before or after conversion. Additionally, our longitudinal analyses, with up to 14 years of data for some individuals, are very robust for detecting small changes in clinical chemistry values. Longitudinal analyses, limited to the lipid profile and liver enzymes, showed that cholesterol values were lower when the powdered form of PFNA blend was used, but that cholesterol values increased when PFNA was used as suspension. This could be consistent with the interpretation that, as in rats, exposure reduced cholesterol levels. However, given likely very low PFNA exposures when used as suspension, no effect on cholesterol would be expected and the observed non-significant increasing cholesterol trend may be a coincidence or attributable to unmeasured variable differences in the group.

PFNA surfactant blend is used, to our knowledge, in two locations in the US, one of which is owned by the sponsor of the study. Given the reasonably large sample size of this study, the negative results most likely represent a null effect of exposure. Additionally, the robustness of the repeated measures longitudinal analysis allowed for examination of clinical results by individuals over many consecutive years. In summary, this study, based on several clinical measures assessed over more

Main messages

- Little is known about the human health effects, if any, of various perfluorinated hydrocarbons. Much attention has focused on perfluorooctanoic acid (PFOA), based on an 8-carbon chain, but no epidemiological data are available on perfluorononanoic acid (PFNA), a 9-carbon compound.
- In an occupational epidemiological study of 630 workers potentially exposed to a PFNA blend, no meaningful differences were observed for any of 32 clinical laboratory measures, including liver enzymes and blood lipids, between employees more likely highly exposed and those believed to be unexposed to PFNA.
- Longitudinal analyses, using repeated measures of clinical outcomes, and controlling for age, body mass index and time period did not modify findings of no differences in blood lipids or liver enzymes.

Policy implications

- This is the first epidemiological study of employees occupationally exposed to PFNA, and with respect to liver enzymes and blood lipids no clinically meaningful differences were observed by category of exposure to PFNA.
- Our negative findings are consistent with the lack of association found in similar studies conducted among employees exposed to other fluorinated hydrocarbons, specifically PFOA, in other industries.

than a decade, has detected no adverse clinical effects from occupational exposure to PFNA.

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